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Clinical contribution of PET/CT in myeloma: From a point of view of radiologist

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Positron emission tomography / computed tomography (PET/CT) using ^{18}F -fluorodeoxyglucose (FDG) has been widely used in various malignancies. It can yield much useful information for staging and restaging, since glucose metabolism is activated in many cancer cells. As for the plasma cell malignancy (PCM), including multiple myeloma, it has been reported that FDG-PET/CT is helpful not only for detecting viable lesions, but for monitoring therapy response and predicting prognosis. Therefore, it is gradually increasing to have an opportunity of PET/CT scanning before treatment of PCM. Durie-Salmon Plus system is currently accepted in clinical, in which magnetic resonance imaging (MRI) and FDG-PET/CT are diagnostic imaging tools for detecting viable lesions [1].

In the National oncologic PET registry data acquired between May 2006 and May 2008, a total of 1784 patients with myeloma underwent FDG-PET scan in US [2]. According to the data, clinical impact on intended management was obtained in about half of the myeloma patients. In addition, a recent meta-analysis demonstrate that the pooled sensitivity and specificity of FDG-PET or PET/CT in myeloma were 61.1% and 94.1%, respectively, in intra-medullary lesions, and 96.0% and 77.8%, respectively, in extra-medullary lesions [3]. It has been also showed that the number of involved lesions was one of the prognostic factors in overall survival and event free survival [4].

FDG-PET or PET/CT images are not always easy to interpret. Since FDG is not a cancer-specific agent, it accumulates in some benign tumors, inflammatory foci or normal organs, resulting in false positive findings. In contrast, some viable lesions of myeloma are not FDG-avid. Sometimes there are cases in which active lesions are not clearly depicted even in spite of high M protein level. Are there any better radiopharmaceuticals other than FDG in myeloma?

FDG is a popular tracer in clinical, visualizing hypermetabolic area of glucose, but since the PCM is characterized by excessive production of monoclonal immunoglobulin, which in most cases can be detected in serum and/or urine, it is reasonable to suppose that an amino acid-based tracer might be useful in PCM. ^{11}C -labelled methionine (MET) is a radiolabelled tracer, which can image hyper-metabolism of amino acid, and has been used for research purpose for many years. There are some articles demonstrating clinical usefulness of MET-PET in differentiating between tumor

recurrence and radiation induced necrosis, or in detecting parathyroid adenoma. Although Dankerl et al. reported the feasibility of MET-PET/CT in multiple myeloma, demonstrating SUVmax (highest standardized uptake value at one single pixel) in myeloma tended to be higher than in normal bone marrow tissue, and concluded that active multiple myeloma can be imaged with methionine PET/CT [5], the clinical value of MET-PET for PCM has not been fully investigated yet. In order to compare the diagnostic performance of MET-PET/CT with FDG-PET/CT, we conducted a preliminary study in our institute, and have recently published our data [6]. MET-PET/CT tended to identify more viable lesions of PCM than FDG-PET/CT did (Figure 1). Interestingly, of 156 lesions evaluated in 20 patients, 60 lesions (38%) had no morphological changes on CT. More accurate results affecting therapeutic management was obtained in just one of six cases in staging and one of 14 cases in re-staging in our population, but MET-PET/CT appears to be helpful especially when FDG-PET/CT findings are inconclusive or undeterminable.

One of the major disadvantages of ^{11}C -methionine PET/CT is its short half-life, i.e. 20 min. For this reason, it cannot be commercially available, and we need to prepare an in-house cyclotron and a synthesizer for MET-PET/CT studies, which is not affordable in all institutes. Recently, one article regarding clinical efficacy of ^{18}F -labelled alpha-methyl-tyrosine (FAMT) for multiple myeloma has been published [7]. FAMT may be more preferable in clinical because FAMT could be commercially available due to its longer half-life (110 min). According to the published data, FAMT uptake in myeloma tended to be lower than FDG uptake, without specific advantages over conventional FDG-PET [7]. However, it is necessary to keep seeking more suitable PET tracers.

We believe that MET-PET/CT as well as FDG-PET/CT would provide useful information for determining a therapeutic strategy of PCM. An inline PET-MR system has been developed, and installed in some institutes. The clinical efficacy of PET/MR has not been established yet, but PET/MR using ^{11}C -methionine may have a significant role in patients with myeloma. To evaluate the diagnostic performance of MET-PET/MR in PCM, further investigations are required. In addition, as an inline PET/MR is an expensive modality, cost-effectiveness should be also discussed in the future.

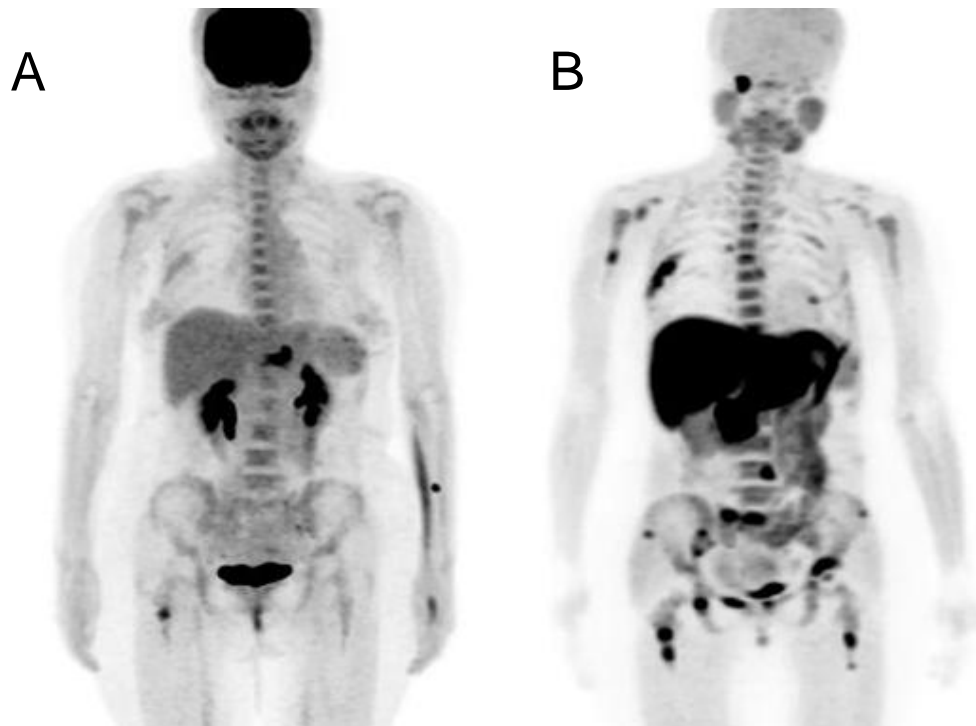


Figure 1.

A 45-year-old female with multiple myeloma. Maximum intensity projection images of FDG-PET (A) and MET-PET (B) are demonstrated. Mild to moderate uptake in the right rib and intense uptake in vertebra and right femur are demonstrated in FDG-PET, suggesting viable lesions of myeloma. MET-PET also reveals viable lesions as hypermetabolic areas of ^{11}C -methionine. More lesions are depicted by MET-PET especially in the pelvic bones and bilateral femurs, which are unclear with FDG. It should be noted that more intense physiological uptake in liver and pancreas is observed in MET-PET, while MET uptake in the brain is faint, compared to FDG-PET.

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